

HEATING TUMORS WITH RF POWER
AND MEASURING THE TEMPERATURE DISTRIBUTION

by

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CREDITS

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ABSTRACT

The goal of this thesis was to provide the thermometry section of a versatile RF power hyperthermia cancer treatment system. By the completion of this project, an experiment was run on egg whites, so the basic elements required for such a system were operable. A number of technical challenges were met, including: A to D conversion with the two grounds isolated, and determining what system topology and algorithms would be most beneficial.

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PROJECT MOTIVATION

Cancer, combining all of its various forms, is the second largest cause of death in the United States, after heart disease. One out of four North Americans will get cancer in their lives, and two-thirds of these will die of it. Annually, a quarter of a million diagnosed cancer patients of the total 850,000 cannot be cured by radiation treatment. We are joining with a multitude of other research efforts in trying to tackle this disease; hopefully, people will soon be able to survive what currently is a fatal disease. Many of these peoples' bodies still have twenty good years left, and making these years a reality is what we are striving for.

How are we approaching the problem? It has been known for quite some time that tumors are particularly susceptible to heat. Hence, research has been examining the hyperthermia treatment of cancer. But this heat treatment requires expertise outside of medicine; the work falls into the realm of engineering. Hence, 'biomedical engineering' comes about. And we in the engineering community have a chance to assist in the health field.

PROCESS OF TUMOR DEATH

A reasonable first question to all of this might be: "How is this treatment able to distinguish the tumor from healthy tissue, to selectively kill cancer cells?" There are three primary factors which answer this:

(1) We use localized heating. That is, we can heat where the tumor is, by tailoring the geometry of the electrodes to the tumor, and stereotaxically inserting the electrodes.

(2) Bloodflow would work against us, since it carries off excess heat, and tends to make body temperatures uniform. But tumors grow quickly, and are not meant to be there. So, blood vessels do not profuse the tumor as thoroughly as they profuse healthy tissue. This lack of bloodflow works in our favor. For chemotherapy, this effect actually hinders the treatment, since bloodvessels are needed to deliver chemicals to the tumor.

(3) The pH in a tumor tends to be somewhat different than in healthy tissue. Fortunately, cells in this different pH environment find it harder to survive the heat treatment.

We can use several drugs to take better opportunity of these advantages, too. Vasodilation can be fought with one drug, and the existing pH difference can be favorably accentuated with another. A factor working against hyperthermia is 'thermal adaptation.' That is, the cells that survive may be the ones able to survive heat better, making it difficult to destroy them with later treatments. It is analogous to insects adapting to pesticides, or bacteria adapting to antibiotics.

Results have shown that 50-90% of the cells die during a one hour treatment at 43°C. Also, a temperature of just 1°C less can make a tenfold difference in cell survivability.

When the biochemistry of the cells is examined, these results are understandable. Basically, cells are not built to take this high temperature. Our bodies are designed to hold the

temperature within a narrow range, through a variety of mechanisms (for example, we get flushed and sweaty when we are hot with fever or hard work). So, if our body temperature does rise, there are a multiplicity of effects. The most critical is the irreversible denaturation of enzymes. In this denatured state, the enzymes are unable to perform their function of catalysis. This is an irreversible effect. This is important, since almost every cellular process requires enzyme catalysis along its pathway. For example, experiments show that cellular respiration is disturbed. An independent result of heating is that lysozomes are liberated, which work to destroy the cell.

Finally, there is another effect that originates at the cellular level, but effects the entire system. In some patients, fragments escape into the bloodstream, which cause the immune system to fire up and respond in full force. In some cases, people have received treatment for just one of a number of tumors, and many of the tumors die — just from the highly stimulated immune response!

We can also combine this heating with various other cancer treatments. The advantage is this: the treatments all have effect on both the tumor and on some healthy tissue. Chemotherapy, for example, often attacks growth processes in general, since growth is a prime characteristic of all tumors. In combined treatment, the advantage is this: each treatment technique used does not have to be used as heavily. Hence, the patient's healthy leg muscle, which might be trying to grow too, will not have to take as much abuse. So, combined treatment can be less harmful to healthy tissue.

Moreover, using a combination of therapies can be more detrimental to the tumors. In mice, the results of radiation treatment were 4 times better when the tumor was put through heat treatment first.

HYPERTHERMIA: APPROACHES AND DIFFICULTIES

Here is a summary of approaches to hyperthermia:

| TECHNIQUE | ADVANTAGES | DISADVANTAGES |
|-----------------|---|--|
| Ultrasound | <ul style="list-style-type: none"> + Non-invasive + Can focus the waves, to get greatest heat at medium depth. | <ul style="list-style-type: none"> - Bones absorb this energy, and that is painful. - You do not know the actual temperature during treatment, except by empirical data. - Mismatches in tissue characteristics cause boundary reflections (eg, at lung, fat-muscle, on surface). |
| Microwave | <ul style="list-style-type: none"> + Theoretically, gets fairly uniform heating. + Field patterns can be directed. | <ul style="list-style-type: none"> - Water absorbs this energy a lot (like in a microwave oven) so muscle heats a lot. - It is invasive. - Temperature only known by empirical data. - Inhomogeneities create hazards, since reflection could cause undetected heating in good tissue. |
| Radio Frequency | <ul style="list-style-type: none"> + Can monitor highest temperature (for safety). + Can get accurate heating. + Can treat deep-seated tumors. + Heating can be directed. | <ul style="list-style-type: none"> - Invasive. - "Hot spots" at the electrodes. - Inhomogeneities: $\sigma_{\text{fat}} = \frac{1}{3} \sigma_{\text{skin}}$ $= \frac{2}{3} \sigma_{\text{viscer}}$ |

RF heating is the method we are using. 500 kHz is low enough to avoid capacitive heating effects, and high enough to avoid causing muscle twitches or initiating other nervous activity.

From the chart, it is clear that every method has the disadvantage presented by inhomogeneities, and that disadvantage itself has a varying degree of importance. It is not clear, but each of these techniques may be most practical for different types of cancer. An additional technique which is being tested

is the use of a ferromagnetic paste, which could be injected and then heated inductively.

SYSTEM OVERVIEW / SCOPE OF THESIS

Now we move on from the theory of cancer therapy to the system we developed for doing the heating. Some RF heating systems have been developed in the past, but there were various disadvantages with each. Also, we wanted to move on to test new geometries of electrodes and switching algorithms. So, we wished to develop a flexible system, which would allow us to test these various hypotheses. Figure 1 shows a block diagram of the current arrangement, which serves the following needs:

| NEED | SOLUTION |
|---|---|
| Deliver power to, ground, or disconnect any electrode, for monopole or dipole heating. | Switching circuit under software control. |
| Measure the temperature at every electrode for feedback. | Thermometry system. |
| Respond to operator control. | Apple®. |
| Show the operator what the system is currently doing; give hard copy record of treatment. | Apple. |

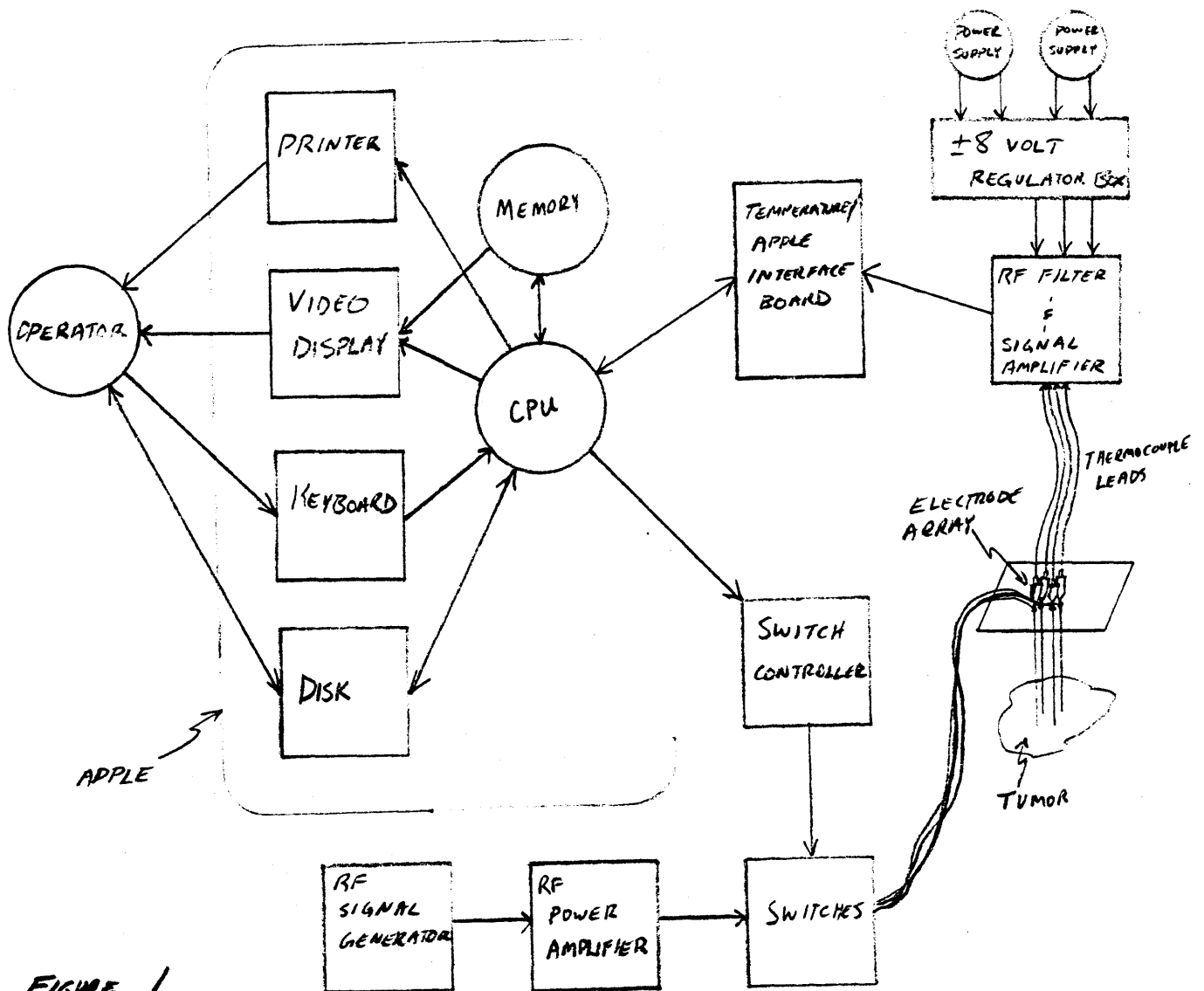


FIGURE 1

Some earlier systems used a 'round-robin' scheme in their heating; this means that any given electrode would be powered up only when its time came around. The disadvantage of this is the large 'thermal ripple.' The temperature always drops off and is boosted exponentially, but these temperature dips are large in magnitude. Our system will hopefully provide more constant heating, and use no more total power.

My thesis work includes the design, building, and testing of the entire thermometry system (except the boards for

the thermocouple amplification and RF filtering, which are off-the-shelf components), writing the Apple programs, and helping to integrate the entire system.

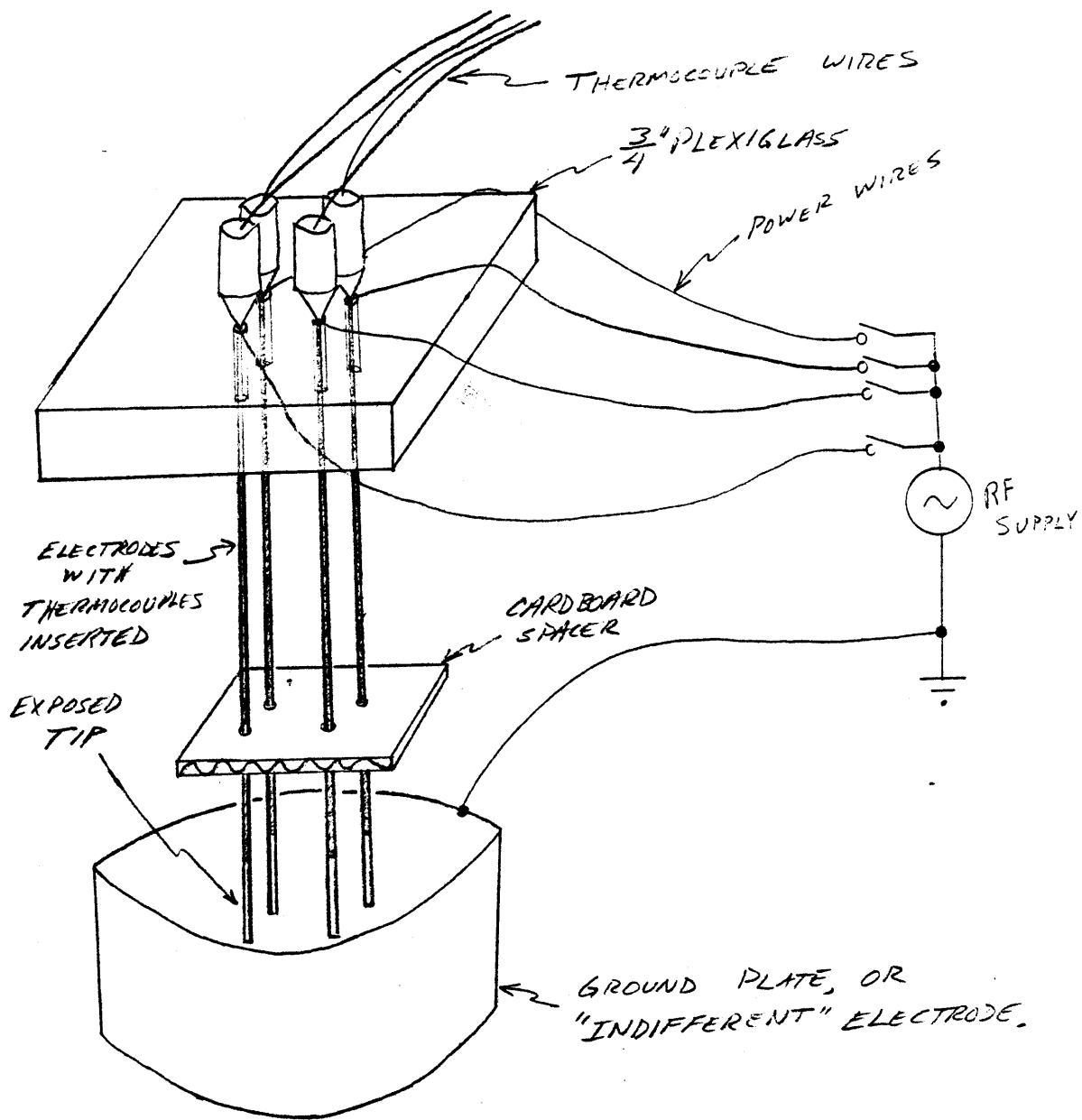


FIGURE 2

HOW THE SYSTEM WORKS

Introduction

In discussing the details of how the thermometry system works, we will start at the tumor, and trace the signals back to the computer.

A. The Electrodes

In clinical use, an array of needle electrodes will be used in heating up the tumor. Power will be driven through these electrodes, into the tissue, and to a ground plate on the surface of a person's body. In our experiments, this was approximated by a simple array of four 18-gauge electrodes delivering power through an egg white media, as shown in figure 2. Egg white is a protein, which means it is of biological nature.

As currents flow through the media, power is dissipated in it. This power is manifested as heat. The heating is primarily resistive, like a toaster coil heating up when it is plugged in. In this case though, we used 500 kHz as the frequency (that is on the low end of the RF spectrum), rather than the 60 Hz that comes from a wall outlet.

Viewed from above, the current flows radially:

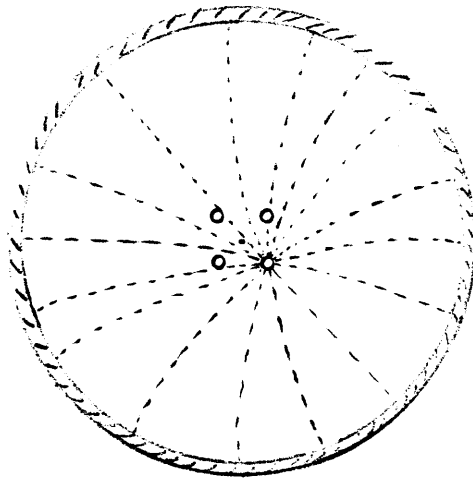


FIGURE 3

Notice that other electrodes are perpendicular to the field lines (or current pathways), so that the field is not disturbed by them. Also, according to this geometry, the current density drops off as $(1/r)$, as we move away from the electrode. This can be easily deduced from these 2 facts:

- (1) Every cylindrical volume positioned around the exposed tip, regardless of radius, has the same total flux leaving it (say, I amps).
- (2) The current density is evenly spread over this cylinder's surface (ignoring fringing fields), and this surface increases proportionally to r .

Heating can be determined by power dissipation. To find that, we square the current density and throw in a proportionality constant, $1/\sigma$. So heating drops off as $(1/r)^2$:

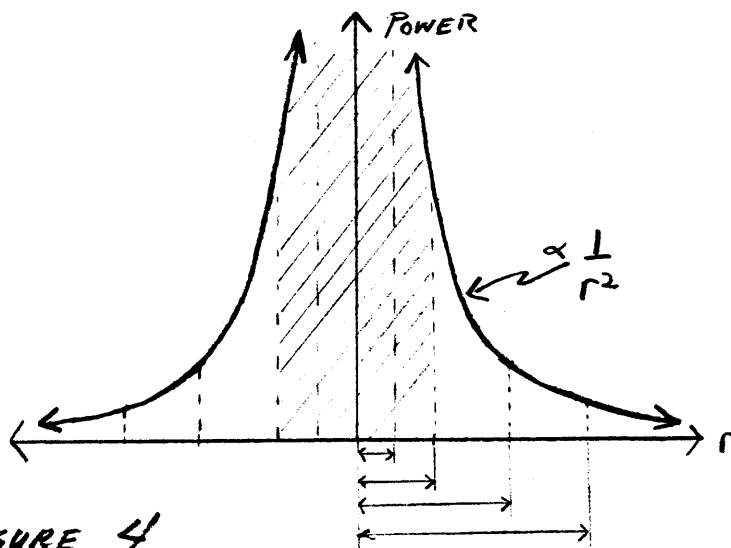


FIGURE 4

Here, various electrode radii are suggested. The power inside the radius of any given electrode has no physical significance. The power right at the surface, and how it drops off beyond that, is the critical consideration, since uniform heating of the tumor is desirable.

It is clear from the graph, then, that the electrode should be as big as possible to avoid excessive temperature peaks at the electrode, which would leave insufficient heating between the electrodes of the array.

It should also be noted that these results only apply to this "monopole" arrangement, where a single source is considered, and the sink is effectively at infinity. Another possible arrangement gives a "dipole" pattern where a nearby electrode is grounded. In that case, heating occurs at both electrodes. This is important when we consider what it means to turn an electrode "off". We cannot ground it; that would

provide a sink. Rather, the electrode must be made a high impedance pathway to RF when it is off.

B. The Thermocouples.

A device is needed to monitor the temperature at each electrode. We used thermocouples. The thermocouples slip inside the hollow electrode, down to the electrode's tip, as shown in figure 5. The temperature is therefore read right at the electrode, where the temperature is highest.

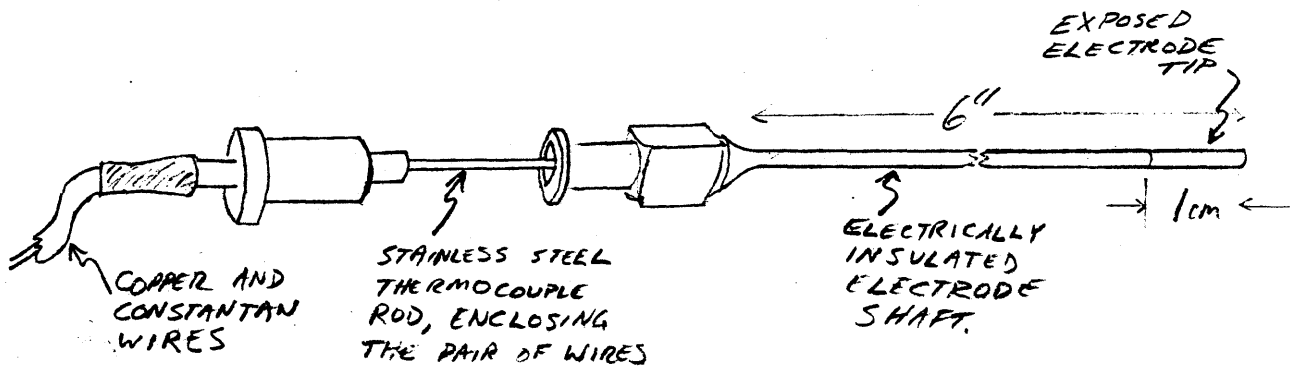


FIGURE 5

A thermocouple is itself no more than a junction between different metals. We used constantan (a copper-nickel alloy) and copper wires, welded together. From the physics of the metals' electron gap, a voltage difference appears across this junction. This voltage changes with temperature, which is the key to its usefulness as a thermocouple. The relationship is linear up to at least 1200°C , where the voltage reaches 50 mV.

C. The RF Filter/Signal Amplifier Box.

It is clear, then, that this voltage is quite small, and must be amplified. Furthermore, the amplifier cannot draw too much current from the junction, or else the relationship would lose its validity, and the whole effort would be futile. So, the amplifier must have a high impedance input.

The output of the amplifier provides a voltage between plus and minus 8 volts. The amplification can be adjusted both in magnitude and in DC offset, to allow calibration of voltage with temperature. This calibration is explained more fully in Appendix A. The output of this amplifier is the voltage actually sent to the computer for temperature monitoring.

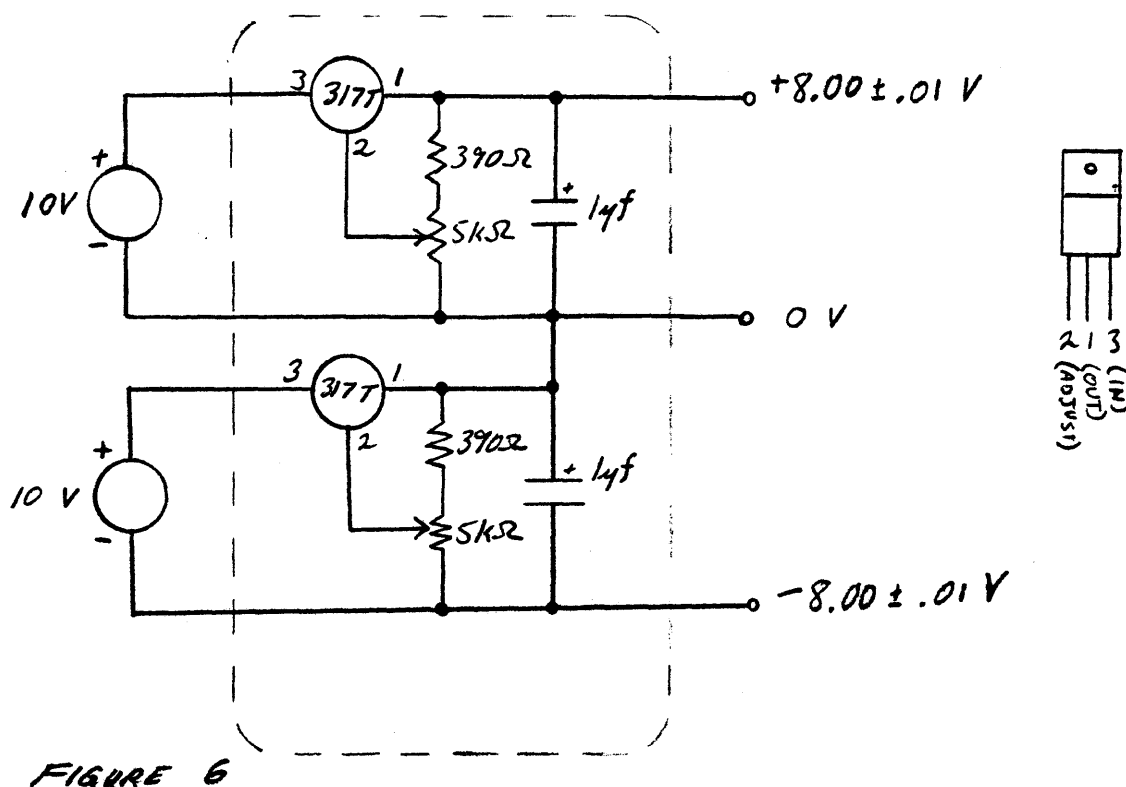
It should be noted that this RF Filter/Signal Amplifier Box contains 8 printed circuit boards; one dedicated to each thermocouple. Currently, the limitation of the entire system is 8 thermocouples.

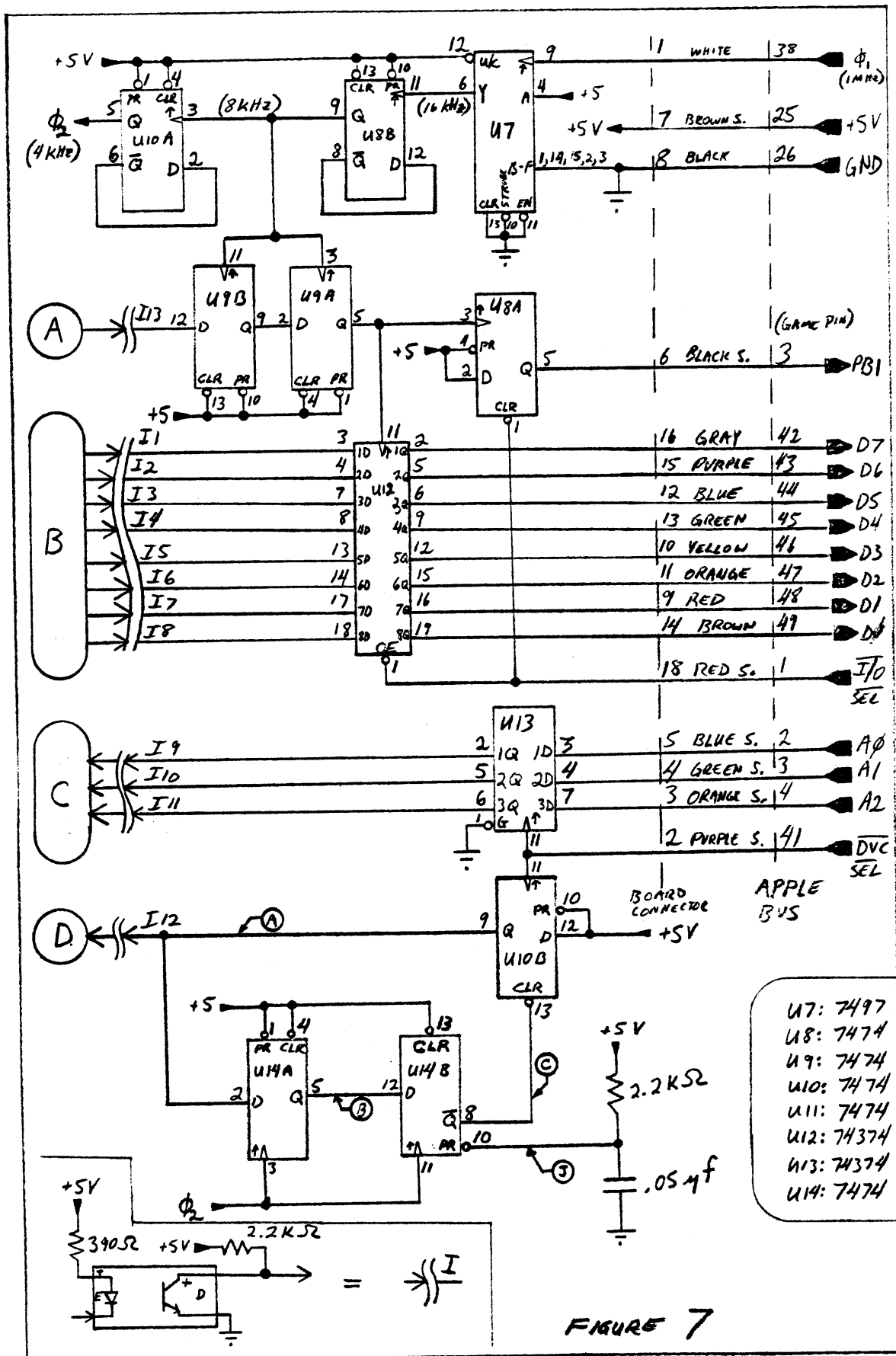
Each of these boards has another feature, apart from amplification; they block out RF current. The thermocouple, then, does not provide a pathway for the RF power which is at the electrode, and the signal that represents temperature does not have an RF component on it. The filter is comprised of a low pass filter and a notch filter, which is tuned specifically to 500 kHz.

Two power supplies provide plus and minus voltages to these amplifier boards. The voltages are carefully regulated at 8.00 volts, to provide the consistent amplification required for accurate temperature readings. The output voltage can be adjusted to stay within .01 volts of the desired value, using

potentiometers. The schematic is shown in figure 6. The two voltage sources are connected plus-to-minus after regulation, to provide both positive and negative voltages, with respect to the system's own 'white ground.' The supplies float with respect to earth ground, so there is no DC pathway into the thermocouple circuit by this route.

It is important that no such pathway exists. If one did exist, both direct current and 60 Hz ground loop currents could flow in the thermocouple leads, creating extraneous voltage potentials.





D. Temperature/Apple Interface Board

This board is the next piece of the thermometry system. In general terms, this board allows the Apple computer to sense the level of any of 8 analog signals. Furthermore, it keeps the ground for the analog side independent of the Apple ground, using 'opto-isolation.'

An opto-isolator is just a light emitting diode and a light sensitive transistor inside a single package. Information is carried from the emitting side to the detection side with light only; there is no electrical connection. In this application, digital signals are transferred, since analog signal amplitude cannot be transferred accurately.

The specific usefulness of this board in the thermometry system is:

- (1) to enable the Apple to request the temperature from any of the 8 electrodes;
- (2) to convert that particular temperature (represented by a 0 to 5 volt analog signal coming from the amplifier box) to something the Apple can understand; and
- (3) to avoid having any connection between the thermocouples and earth ground.

So, the purpose of this board, and the importance of its features, should be clear.

We will move on then, to how it works. Figures 7 and 8 show a full schematic of this interface board. There are a number of general sections which comprise the whole circuit. The key chip is U1, the ADC 0808. It receives the 8 analog inputs, multiplexes them to choose 1, converts the signal to digital form, and has a register on the output to hold the answer. If the isolation were not needed, this and an inverter

would complete the circuit.

As it is, several other sections are required, all because the opto-isolaters perform slowly, as compared to the Apple and the ADC 0808. Other methods of isolation are available, and can be implemented at various stages of the circuit, including the analog inputs. However, opto-isolators are relatively inexpensive, and still fairly quick.

Typically, before the opto-isolator can even turn on or off though, the Apple has already been through 100 complete clock cycles (at 1 MHz). This means that all signals travelling from one side to the other must be set up and held for quite a while, until the information has a chance to get through. Hence, both (1) the data, and (2) the signals that indicate when this data is valid (that is, DVC SEL and End Of Conversion) must be extended. U1 and U13 perform this 'set-up-and-hold' function for the data being passed, as U16b, U14, and U1 do this for the 'indicator' signals.

Furthermore, once the indicator signals get across, they must wait some extra time before declaring officially that all the data has arrived, since it may not have. That is, since the opto-isolators do not have uniform delays, and more particularly since turn-off time is less than turn-on time, some signals will arrive on the 'secondary' side sooner than others. This required wait-time is provided by U3f and U2d, and with U9 and U8a. Then, the data is sure to be valid, and can be latched by U12 and U1.

Another consequence of the opto-isolator delay is that the whole concept of running synchronously (that is, events

happening simultaneously) loses its meaning. Basically, transmitting clocks across these isolators would be futile. This explains the need for the independent crystal oscillator, Y1, on the floating side of the circuit.

Special sections are also needed just to divide down the clock speeds (U7, U8b, and U16a; and U3a, U2c, U15a, U6, and U4b). That explains how the circuit's various sections generally fit together.

Now, an illustration is in order. We will follow through the reading of a single temperature, and see how various signals behave. The process begins in software, to initialize before reading:

1. We PEEK at location 49152+1024, which
2. causes the CPU to 'read' from that address (50176), which
3. causes $\overline{I/O\ SEL}$ to drop low at slot #4, where this interface board is connected (this action is documented in the Apple II Reference Manual), which
4. clears U8a, which
5. makes sure that PB1 is low.

Next, we have to set up to read from a particular thermocouple. Take thermocouple #5, for example:

1. We POKE 49280 + 64 + 4, X, which
2. causes the CPU to write to address 49348, which
3. causes $\overline{DVC\ SEL}$ to go low, and A0 = 0, A1 = 0, and A2 = 1. (That is 100 in binary, or 4, for the thermocouple number. We start counting at 0 for this, so 4 indicates thermocouple #5.)
4. Then, the following timing patterns occur on the interface board:

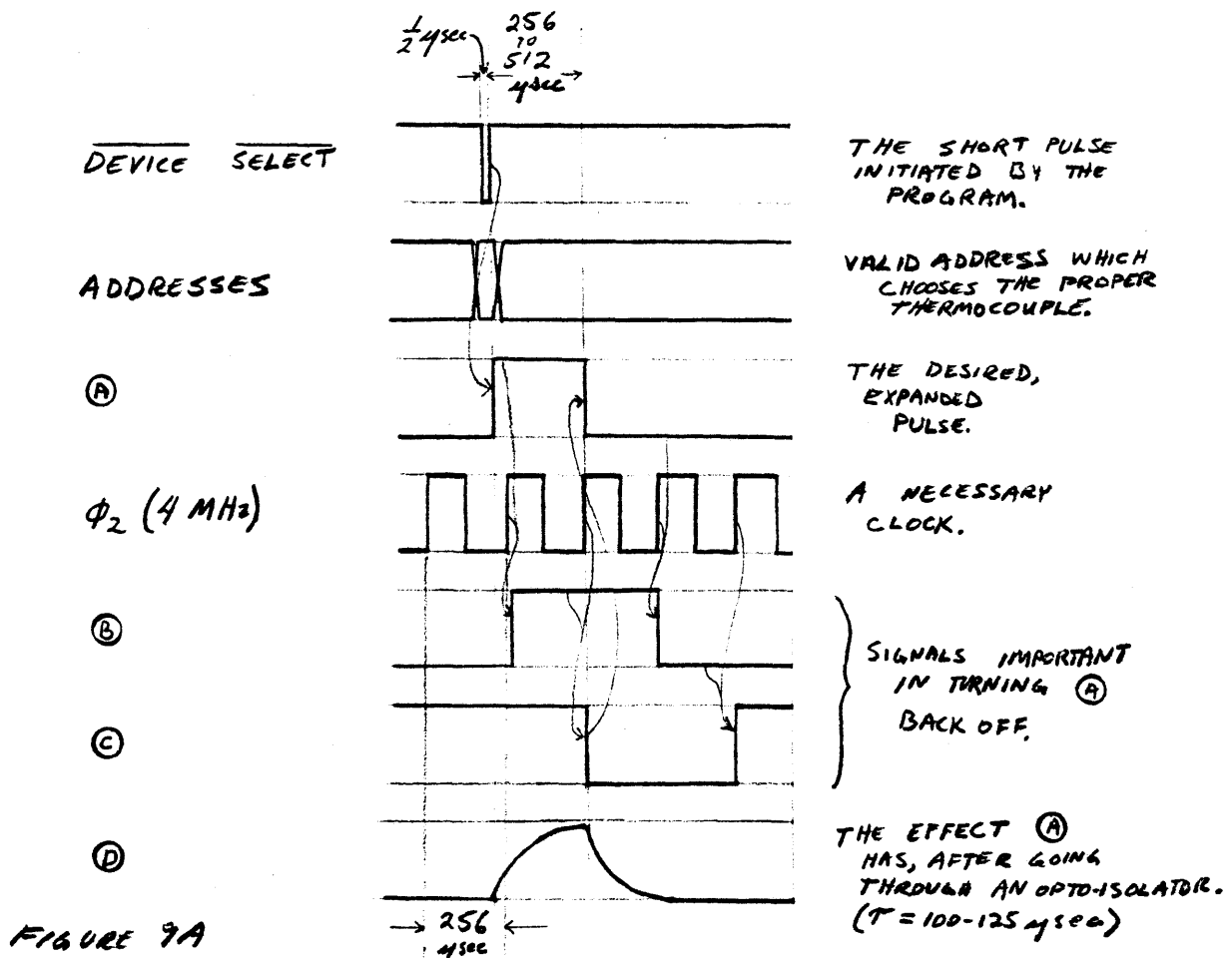


FIGURE 9A

So, the appropriate signals have been stretched enough to get across the opto-isolator. Notice that the Apple's clock must be divided down enough to provide a sufficiently wide pulse in place of **DVC SEL**. This is done by U7 (which divides the frequency by 2^6 , or 64), and U8b, and U16a (each of which divide it in half).

The signal is then recovered on the other side, and properly manipulated for presentation at the chip itself:

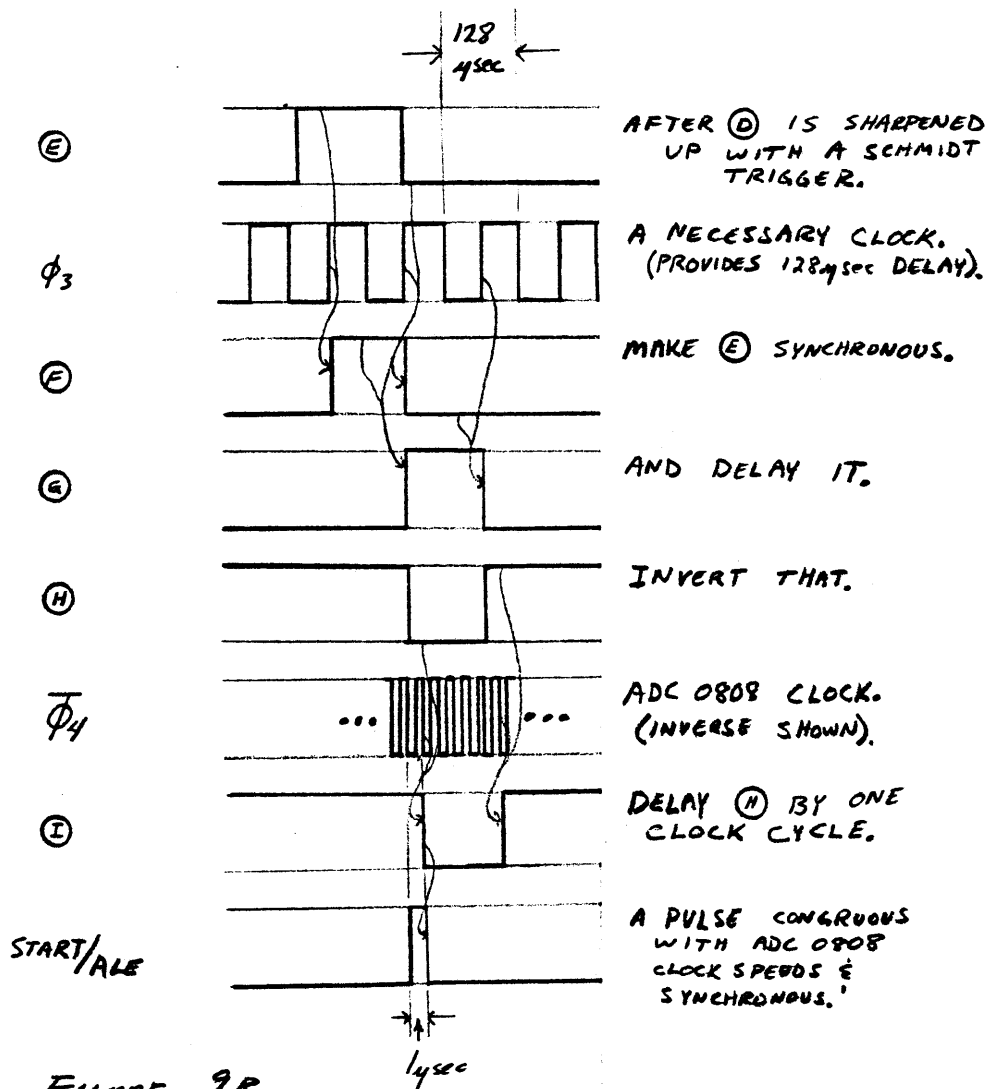


FIGURE 9B

The timing of the Start/ALE pulse is critical. Its leading edge latches the thermocouple number. Its trailing edge, which comes 1 μsecond later, tells the conversion to start (in this case, on analog input IN4), in accordance with ADC 0808 specifications. The pulse is generated whenever (G) transitions from low to high. The logic, in words, basically says 'make Start/ALE go

high whenever © is high now AND low 14second ago.'

The A/D conversion that takes place follows a formula:

$$\text{DATA OUT} = \left[\frac{(IN_4 - V_{REF-})}{(V_{REF+} - V_{REF-})} \cdot 2^8 \right] = \left[\frac{IN_4}{V_{REF+}} \cdot 256 \right]$$

FUNCTION OF
SINCE
A/D CONVERSION
 $V_{REF-} = 0 \text{ VOLTS}$

That is, it makes a digital representation of the analog input, with 8 bits of precision. The analog inputs are limited to a range of -0.6 to +5.1 volts by the use of diodes and zener diodes, not shown in the schematic. The conversion is a process of successive resistor-divider network guesses, and voltage comparisons, internal to the 0808. When it is complete, two things happen: (1) the 8-bit output becomes valid with the digital answer, since the output is always enabled on U1; and (2) EOC (End of Conversion) goes high. These signals are all fed directly into opto-isolators.

On the other side, now, the timing is fairly straight forward. U9a and U9b synchronize EOC and delay it by 128 4seconds. This is again required because of differences in opto-isolator response time. The rising edge of the delayed EOC causes the latch, U12, to grab the data at its inputs and also triggers U8a to assert PBl (pushbutton #1) high.

This pushbutton signal is what the computer has been waiting for all along. Now the program knows that U12 contains the information required to calculate the temperature value.

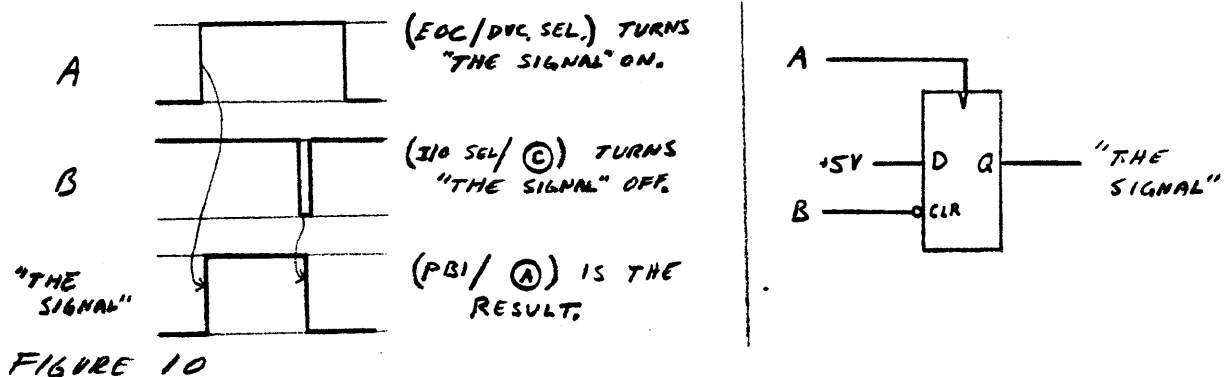
So, it:

1. reads from location $49152 + 1024$, which
2. causes $\overline{I/O\ SEL}$ to go low, which
3. restores PBI to a 0 for next time, and enables U12's output. That is, U12 goes from a high impedance state (where it does not influence the data lines to go either high or low), to a state where it asserts the data value onto the bus, and
4. the computer is able to read this data byte, just as though it were reading in a byte of data from memory.

For this interface board, there are several other

explanatory notes:

- (1) Flip-flop U8a is configured so that PBI is set by EOC's rising edge, and cleared by $\overline{I/O\ SEL}$ dropping low:



- (2) (A), similarly, is set by $\overline{DVC\ SEL}$'s rising edge, and cleared when (©) drops low.

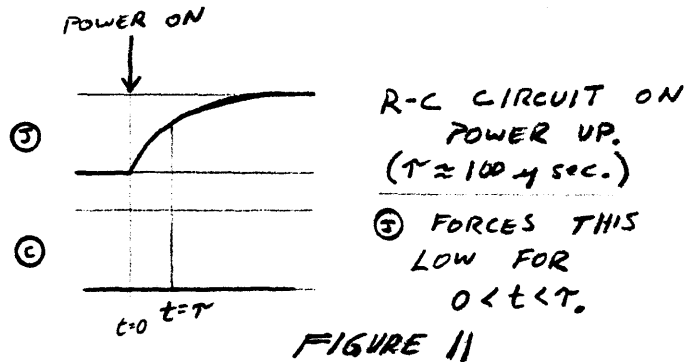
- (3) Only 7 chips and the opto-isolators need to be powered by the Apple's +5 volt supply.

- (4) There is a power-up circuit which assures that (A) is initialized to zero when the computer is turned on. It is the resistor-capacitor combination on U14b. The capacitor charges from 0 to 5 volts with time constant

$$\tau = RC = (2.2 \times 10^3)(.05 \times 10^6)$$

which is about 100 μ seconds. This causes (©) to be low at

this early time, which clears the flip-flop U16b.



(5) The board is powered in two ways. The half that floats does not get its power from the Apple. It uses the same ground and power as the amplifier box does. It must regulate the +8 volts down to +5 volts, though. Two separate regulators supply the circuit as a whole, and the $V_{\text{ref+}}$ input to the A/D converter. This insures a stable reference voltage.

Also, capacitors are needed across the voltage supply lines. Without them, the regulators cause a high frequency oscillation. The capacitors effectively short out that high frequency component, and eliminate it.

E. What the program "THERMO" does.

Now we have a computer that can read in temperatures.

To summarize, the basic software steps it takes to read a temperature are:

1. 'X = PEEK (\$CnXX),' which clears PBI with $\overline{I/O SEL}$.
2. 'POKE \$CO(8+n)m, X' tells the chip to read thermocouple number m, using $\overline{DVC SEL}$.
3. Keep PEEKing at \$CO6k until bit 7 comes on, which indicates that the end of conversion has come.
4. 'TM = PEEK (\$CnXX),' which gets the value for temperature, using $\overline{I/O SEL}$.

Here: 'PEEK' means 'read from location ...'
'POKE' means 'write X to location ...'
\$ indicates a hexadecimal number (that is, base 16)
n = slot number (0 to 7)
m = thermocouple number (0 to 7)
k = push button number (0 to 3)
'X' means the value of the digits does not matter.

That is the most special part of the program.

The rest of the program is typical BASIC programming.

It stores this data and allows the user to display it in various ways. For example, the calibration plots in Appendix A are the result of THERMO. Those plots represent the temperature of all the thermocouples plotted out over time. In this instance, many thermocouple temperatures are shown on a single plot, to allow us to compare them. Also:

- (1) plots can be made individually,
- (2) calibration dots can be added, to make it easier to read temperature values directly from the plot, and
- (3) plots can be obtained in hard copy by using the 'print' command, which dumps the contents of the screen onto the printer.

All of these commands are single keypunches, and are displayed to the user at the base of the screen.

Another feature of THERMO includes looking at the 8

thermocouple temperatures side by side, in real time. It is similar to looking at 8 mercury thermometers, with a numerical display of the temperature values along the base of the screen.

This program is able to acquire one data point each second, store it, and display it. It can display 240 such points, for a total of 4 minutes' worth of data. Along with some short diagnostic programs, THERMO was used primarily in hardware development and in calibration. A full listing is given in Appendix B.

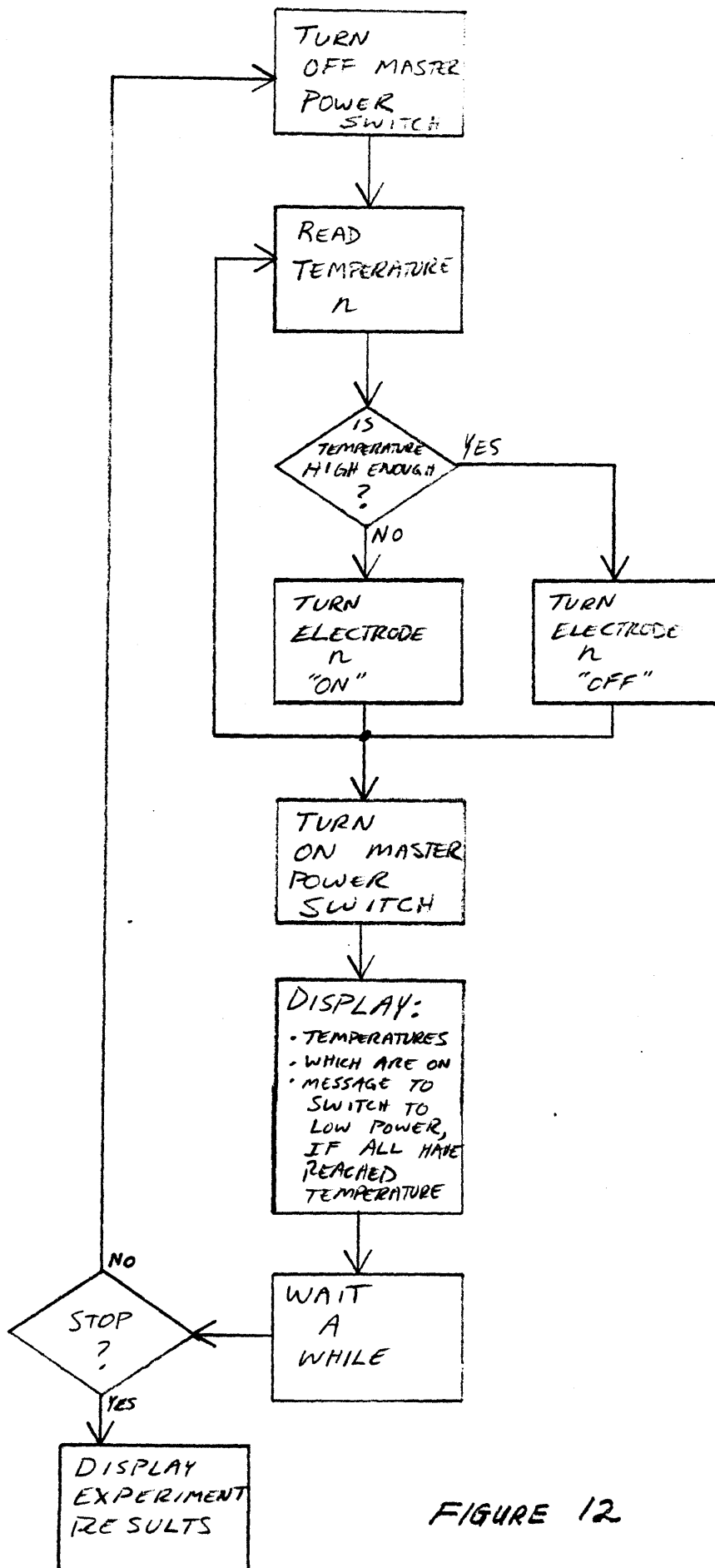


FIGURE 12

F. What the Program XPRMNT Does.

This program has many of the routines found in THERMO. It has a completely new section though, too, which conducts a heating experiment. After this experiment is complete, plots can be made to examine the results. The plotting capabilities are similar to THERMO.

A flowchart of this program is shown in figure 12. Notice that we can control power at each of the electrodes independently. An RF power switching circuit provides this capability. Basically, heating is applied (for one second at a time) to any electrode which is cooler than the 'standard temperature,' set to be 43°C in this case. During the heating, 2 conditions are stored and displayed: (1) the temperature of each thermocouple, and (2) which thermocouples are on.

This program was used in the final experiment, in which the heating and temperature feedback systems were integrated and working together. The actual program listing is in Appendix C.

THE EXPERIMENT

The purpose of the experiment was to see the whole system put together and working properly. The electrodes were held in a square array, inserting them through holes in a 3/4" plexiglass block. There was another hole in the center of the pattern to accommodate a fifth thermocouple, with no electrode. This thermocouple just measured temperature, to give us an idea as to what the temperature drop between electrodes is. A piece of cardboard below the plexiglass held the electrodes in place along their whole length, giving about a 1 cm spacing.

We got encouraging results from the experiment. The 2 plots are shown in figure 13. The first shows the plots of all four corner thermocouples, which were inside the power electrodes. The second plot shows all five thermocouples, with the plot of the fifth (center) thermocouple enhanced.

Apparently, the first thermocouple was calibrated incorrectly. It read about 5°C lower than the rest, when examined afterward. So the actual temperature there was about 5°C higher than shown. During the 1 minute, 40 second experiment, the temperature at the center position measured only about 0.5°C lower than the average of those around it.

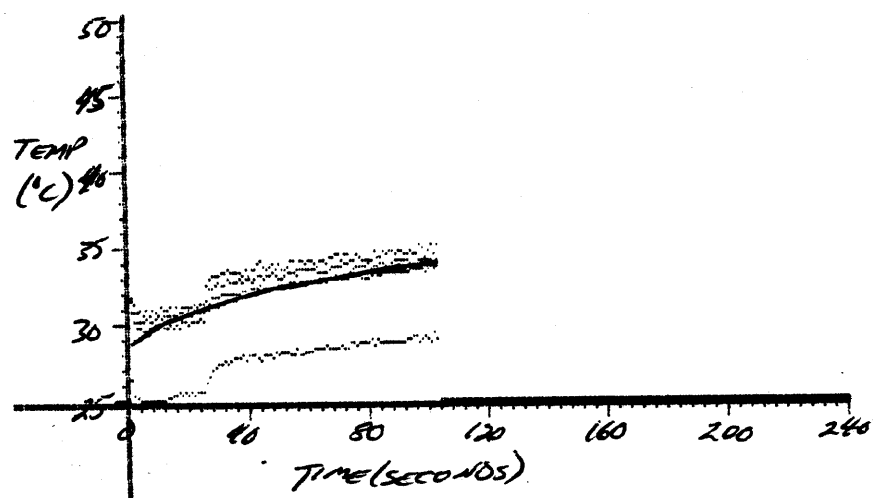
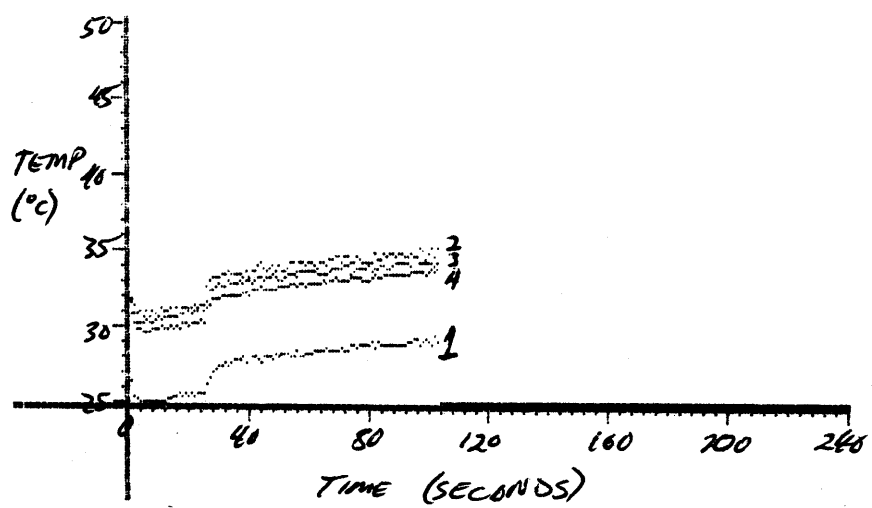


FIGURE 13

DIRECTIONS OF FUTURE RESEARCH

This thesis project provides a skeleton of a system which will require some fleshing out and refinement. There are a great number of enhancements which should be made, both in getting this system closer to clinical use, and in improving its performance once it is there. Here are some:

- A. Most importantly, the accuracy of the temperature measurement should be improved, since the present variability of 1°C between thermocouples at various points is not acceptable.
- B. To come closer to actual clinical conditions, profused tissue should be experimented with as a phantom. One source for organs, such as liver, is Trelegans at 53 Clay Street in Cambridge. It is important to estimate how much effect bloodflow will have in washing out heat between electrodes.
- C. A greater number of thermocouples may be needed. Another 8 could be added with: (1) the corresponding number of amplifier boards; (2) another ADC 0808 and some minor support circuitry; and (3) expanded software to accommodate the extra displays and storage required.
- D. Various new geometries could be examined experimentally, or using mathematical analysis.
- E. The temperature/Apple interface board should be wirewrapped and put inside the main Apple chassis.
- F. Dropping a radioactive seed inside an implanted electrode might be an easy way to combine various approaches to cancer therapy.
- G. If the software seems to be a limiting factor in regard to system response time, the programs (particularly the treatment section of XPRMNT) could be translated into 6502 assembly language.
- H. To reduce the temperature 'ripple,' over time, it may be helpful to rearrange the system configuration somewhat. The response time of the system would have to be reduced. To do this, we could take the Apple out of the feedback loop. In its place, we could design a finite state machine dedicated to controlling a hardware comparator. This comparator could compare the actual temperature at the electrode to a standard, desired temperature, as is currently done in software. Then, it could decide to apply power, or turn it off.

The Apple would still be useful in monitoring the temperatures and the on/off duty cycles of the electrodes. This

is important for safety reasons, and practical in keeping a record of the heat treatment.

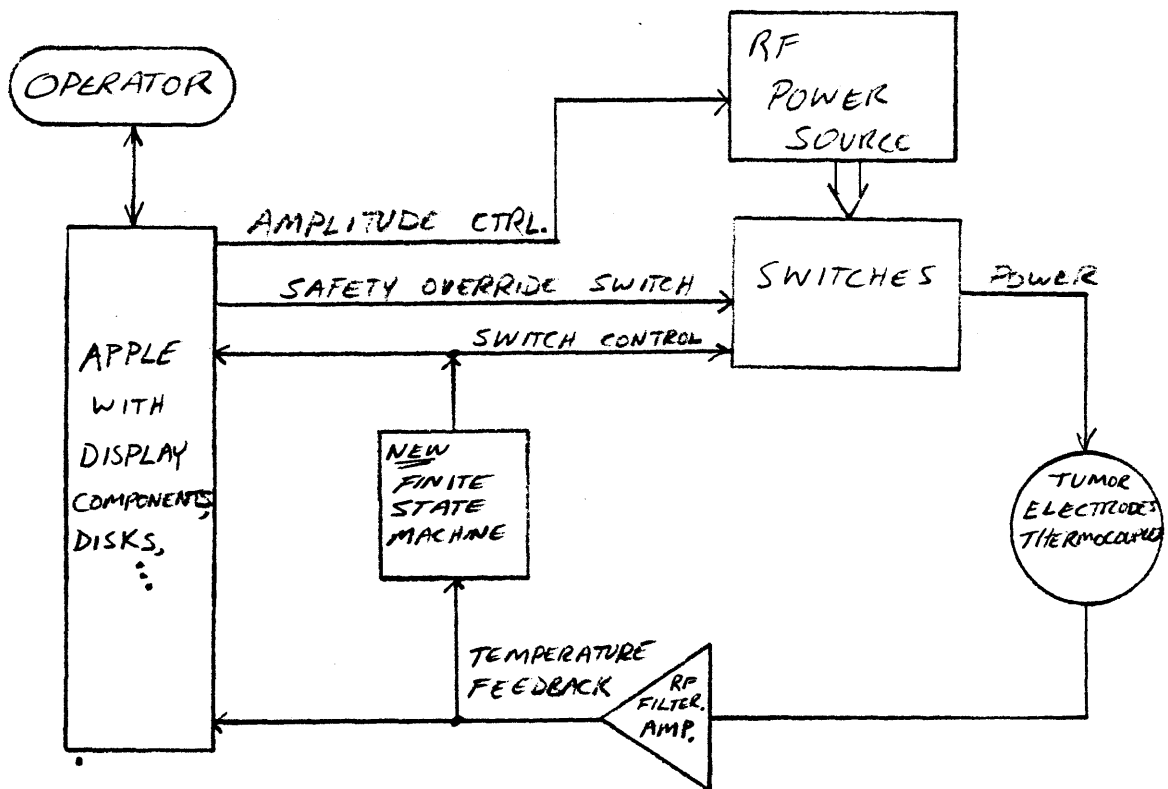
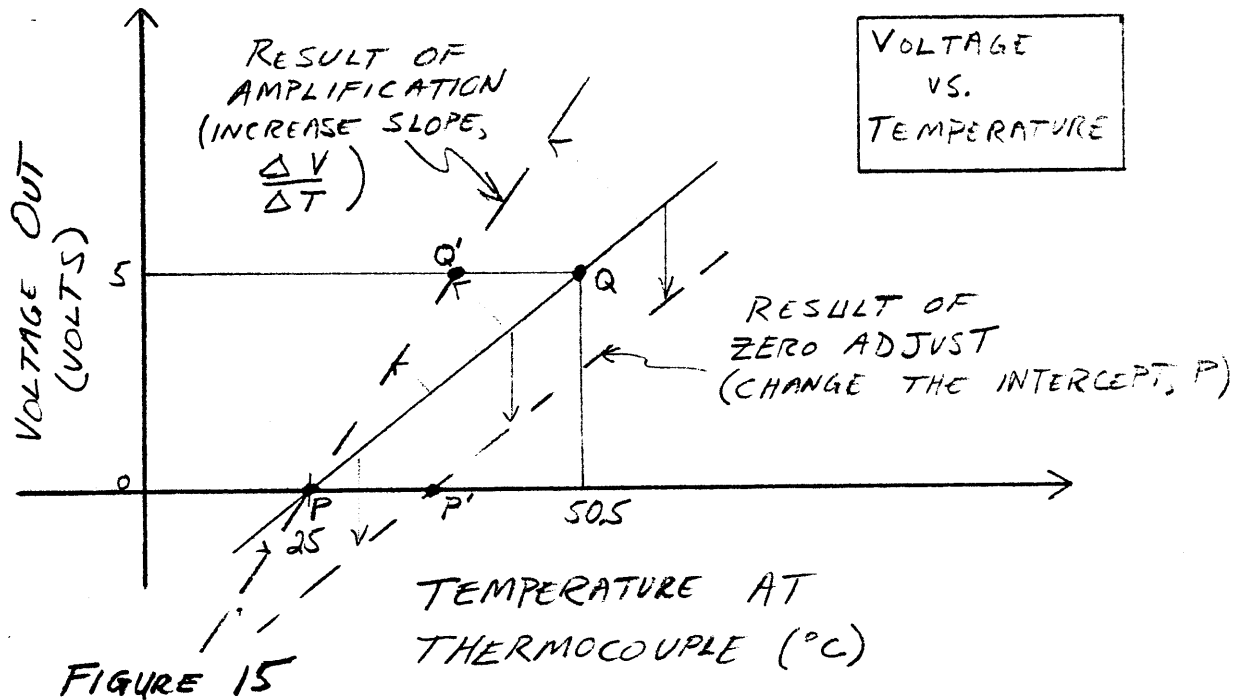


FIGURE 14

This may also solve what may presently be a harmful condition — the switching of RF power at 1 Hz. One team of researchers at the University of California had difficulty with muscle twitches, when they did something similar to this.

APPENDIX A Thermocouple Calibration

The relationship between the thermocouple temperature and the voltage coming out of the amplifier box is linear. The amplifier design allows the 2 parameters of this line to be



Given this flexibility, the 0 to 5 volt output can be adjusted to represent any reasonable temperature range. Since the system can get 8 bits of precision, there is the possibility of 256 discrete temperatures it can detect. A range from 25°C to 50.5°C is possible, with 0.1°C precision. Body temperature is 37°C, and the heating must go up to at least 43°C, so this range is appropriate.

The calibration dictates what the meaning of the plots (like the ones in Appendix A) is, in regard to the markings on the vertical temperature axis. Under the current system, the baseline temperature is 25°C, and large markings go up by 5°C

increments.

To actually calibrate the thermocouples, the following process was followed:

- (1) Set the zero adjust properly. To do this, I put the thermocouples in a 25°C bath, as shown in figure 16, and adjusted a potentiometer to set the output voltage to zero. The location of the potentiometer is shown in figure 17. This is adjusted so the line goes through point P.

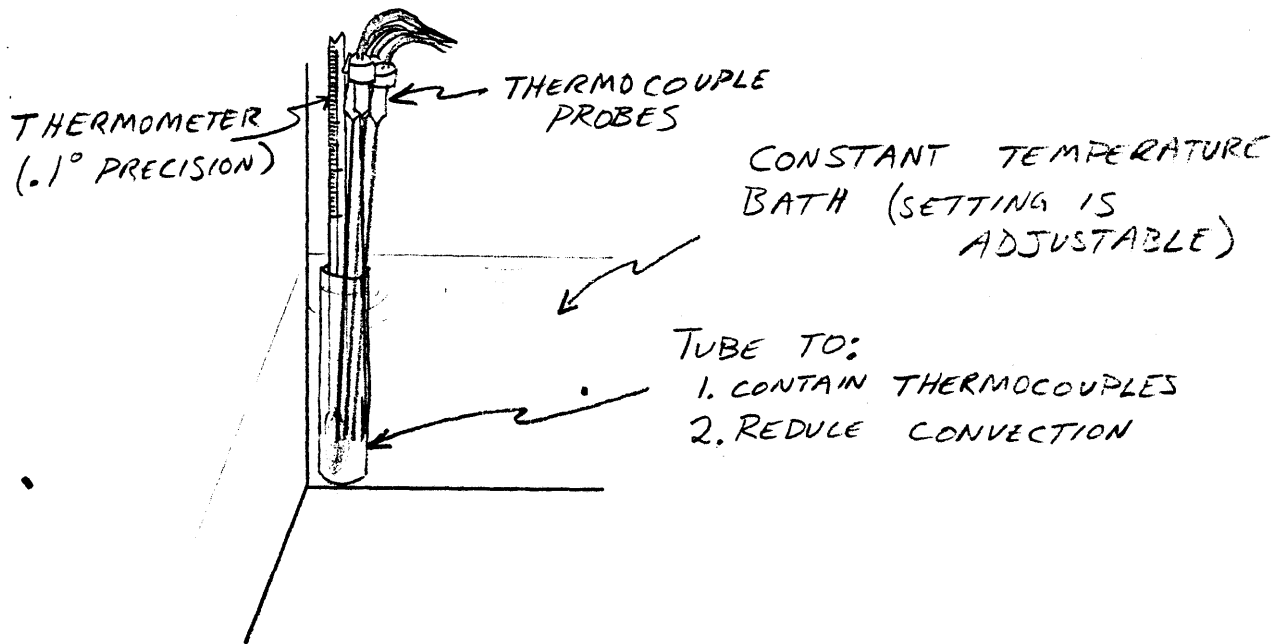


FIGURE 16

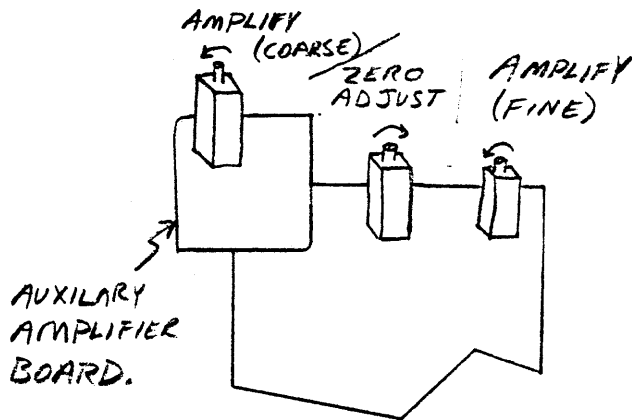


figure 17. Looking at the top of each amplifier board, there are three potentiometers: one to adjust the zero crossing, and two for amplification. The arrows indicate the direction which yields a higher voltage for a given temperature.

(2) Set the gain properly. Adjusting the slope does not affect the 0 voltage intercept, which is already set properly. This allows us to make the line go through point Q. These two points define the desired line.

Once calibrated, the whole set of thermocouples is adjusted consistantly. This was verified by having them track a changing temperature together. This also tests the dynamic characteristics (that is, the response to temperature fluctuations). The resulting graphs are shown in figure 18.

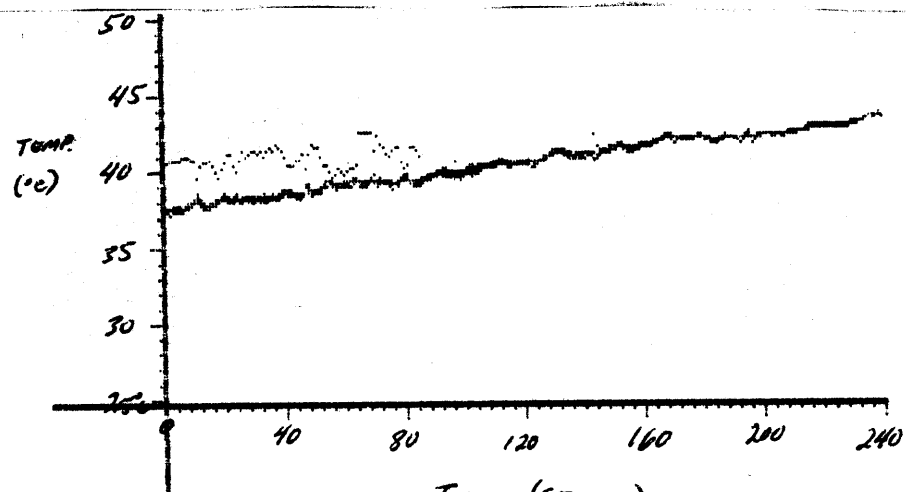
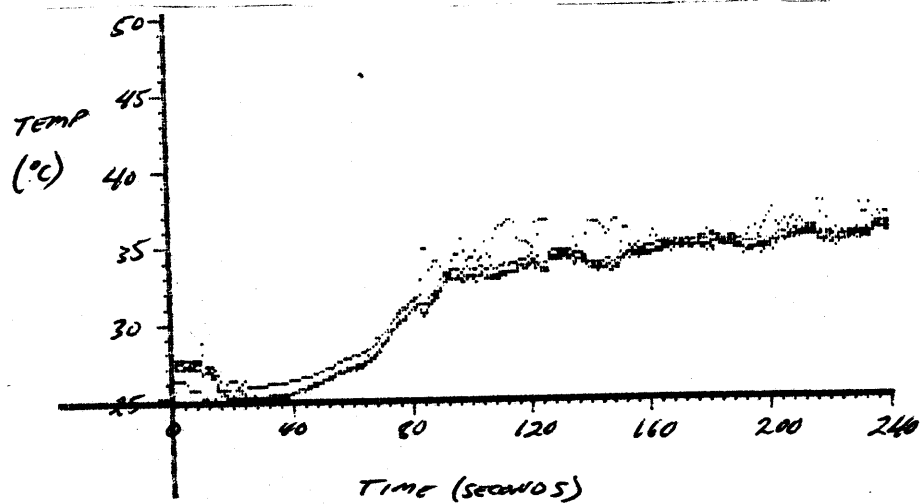
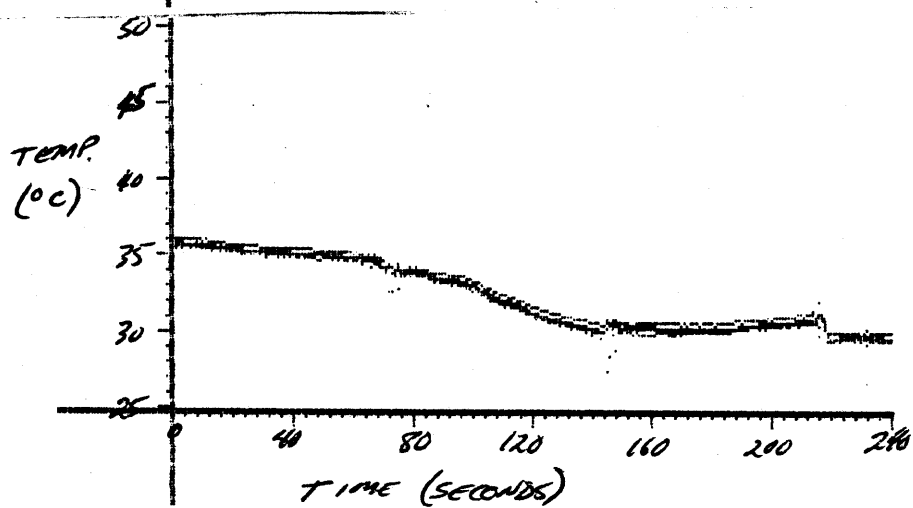
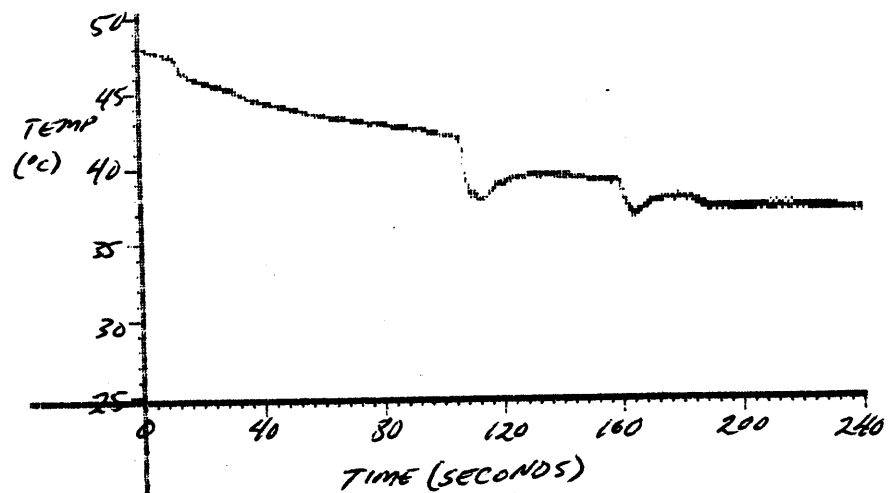


FIGURE 18

APPENDIX B — THERMO

Variable List:

A%(7,239) = Storage array for temperature data. (8 thermocouples, 240 data points).
DS = Allows System Commands from BASIC.
FG = A flag indicating whether in mercury plot or time plot mode.
J = A temporary variable.
K = A temporary variable.
P = The number of the data point we are up to.
PB = Pushbutton number.
PO = Whether to erase old plot before drawing a new one.
Q = A temporary variable.
Q(7) = Not used.
SN = Slot number the interface board is in.
TH = Thermocouple number.
TM = Temperature value.
TN = Number of the displayed plot.
TP = Calculated temperature value (in C).
TP\$ = String holding value of TP.
X = A temporary variable / Keyboard value.
Y = A temporary variable.
Y1 = The temperature value from last time.
Y2 = The temperature value for this time.
Z1 = Screen position for Y1.
Z2 = Screen position for Y2.

APPENDIX B -- "THERMO"

(1)

```
80 LOMEM: 24576
89 :
90 REM INITIALIZE/SET UP SCREEN
91 :
100 TEXT : HOME
110 PRINT "THIS WILL PLOT 8 TEMPERATURES OVER TIME. "
115 PRINT "IT WILL ALSO PLOT 8 PRESENT TEMPERATURES "
116 PRINT "SIDE BY SIDE. READY";: INPUT Q$
132 SN = 4: REM SLOT NUMBER
133 PO = 1: REM WHETHER TO ERASE OLD GRAPH OR PRINT OVER IT
136 PB = 1
138 REM PUSHBUTTON # (THAT IS, FOR THE ONE-BIT INPUT)
142 DIM A%(7,239): DIM Q(7)
144 HGR : HCOLOR= 7: HOME
146 TN = 1: REM # OF THE DISPLAYED PLOT
147 GOSUB 450: REM DRAW AXES
152 PRINT " 1    2    3    4    5    6    7    8
153 PRINT "00.0 00.0 00.0 00.0 00.0 00.0 00.0 00.0";
154 :
155 REM MAIN PROGRAM
156 :
158 FOR P = 0 TO 239
160 FOR TH = 1 TO 8
170 GOSUB 290: REM GET A TEMP
175 GOSUB 2000: REM DISPLAY TEMP
177 IF FG = 1 THEN GOSUB 2200: REM DRAW MERCURY
180 NEXT TH
185 IF FG = 0 THEN GOSUB 600: REM DISPLAY THE NEW POINT
190 X = PEEK (49152): IF X > 127 THEN GOSUB 1000
280 NEXT P: UTAB 23: HTAB 1: PRINT "          DATA BUFFER IS NOW FULL
          ":P = 239
283 X = PEEK (49152): IF X > 127 THEN GOSUB 1000
286 GOTO 283
289 :
290 REM GET TEMPERATURE
291 :
292 REM CLEAR PB FLIP FLOP
293 X = PEEK (49152 + SN * 256)
298 REM START A=>D ON PROPER
299 REM THERMOCOUPLE
300 POKE 49280 + 16 * SN + TH - 1,0
305 REM 49280=$C080, DUC SELECT
310 REM WAIT UNTIL READY
315 X = PEEK (49250)
320 REM 49248=$C060
330 IF X < 128 GOTO 315
340 REM GET THE TEMPERATURE
350 TH = PEEK (49152 + SN * 256)
360 REM 49152=$C000, I/O SELECT
365 :
370 REM AND STORE IT
375 :
380 A%(TH - 1,P) = TH
390 RETURN
```

(2)

```

449 :
450 REM DRAW AXES
451 :
460 HPLLOT 38,0 TO 38,159: HPLLOT 39,0 TO 39,159: HPLLOT 0,128 TO 279,128: HPLLOT
    0,129 TO 279,129
470 FOR Y = 1 TO 60: J = 39 + 4 * Y: HPLLOT J,130
480 IF Y / 10 = INT (Y / 10) THEN HPLLOT J,131 TO J,133
490 NEXT Y
500 FOR Y = 127 TO 1 STEP - 5: HPLLOT 37,Y: NEXT Y
510 FOR Y = 127 TO 1 STEP - 25: HPLLOT 34,Y TO 37,Y: NEXT Y
515 UTAB 21: HTAB 1: PRINT "USE: 1-8, A/T DOTS, X EXITS, R RESTARTS,P PRI
    NTS, 0 OTHER GRAPH,& S. NOW #"TN".
520 RETURN
600 :
610 REM DRAW A NEW POINT
611 :
620 HPLLOT 40 + P,127 - INT (A%(TN - 1,P) / 2)
630 RETURN
800 :
810 REM DRAW A PLOT
815 :
900 FOR X = 0 TO P: Y = A%(0 - 1,X): IF Y > 255 THEN Y = Y - 256
905 HPLLOT 40 + X,127 - INT (Y / 2): NEXT X
910 RETURN
999 :
1000 REM A BUTTON'S BEEN PUSHED
1001 :
1005 POKE 49168,0: X = X - 176
1010 IF X = 34 THEN RUN
1011 IF X = 40 THEN TEXT : HOME : END
1012 IF FG = 1 THEN 2100
1014 IF X < 9 AND X > 0 THEN 1064
1025 IF X = 17 THEN 1400
1027 IF X = 36 THEN HCOLOR= 0: GOSUB 1400: HCOLOR= 7: RETURN
1028 IF X = 35 THEN PO = - PO
1029 IF X = 31 THEN 1800
1030 IF X < > 32 THEN RETURN
1035 :
1036 REM SEND GRAPH TO PRINTER
1037 :
1040 UTAB 1: PRINT " ":D$ = CHR$(4)
1050 PRINT D$"PR#1"
1051 FOR X = 1 TO 20: NEXT X
1052 POKE - 12524,0: REM INVERSE
1055 CT = N
1060 PRINT "THERMOCOUPLE #"TN", 1 SECOND/SAMPLE.": PRINT CHR$(17): PRINT
    D$"PR#0": RETURN
1062 :
1064 REM DRAW A NEW PLOT
1066 :
1070 Q = TN:TN = X: IF PO = 1 THEN HCOLOR= 0: GOSUB 800
1075 UTAB 22: HTAB 35: PRINT TN:
1080 Q = TN: HCOLOR= 7: GOTO 800
1400 :
1410 REM ADD POINTS OF CALIBRATION
1420 :
1430 FOR Y = 127 TO 0 STEP - 5: FOR X = 59 TO 279 STEP 20
1440 HPLLOT X,Y: NEXT X,Y: RETURN

```

```

1800 :
1810 REM SHOW A GRAPH OF ALL THE TEMPERATURES (3)
1820 :
1830 TEXT : HGR : VTAB 21: HTAB 1: PRINT "USE 0 TO GET BACK TO THE OTHER
GRAPH. ";
1835 VTAB 22: HTAB 1: PRINT "USE X TO EXIT.";
1836 PRINT " USE R TO RESTART.";
1840 PRINT : FOR Y = 1 TO 8: FOR Z = 1 TO 2: HPLOT 35 * Y - 25 + Z,0 TO 3
5 * Y - 25 + Z,159: NEXT Z
1850 FOR X = 127 TO 0 STEP - 5: HPLOT 35 * Y - 25,X: NEXT X
1860 FOR X = 127 TO 0 STEP - 25: HPLOT 35 * Y - 26,X TO 35 * Y - 28,X: NEXT
X
1870 NEXT Y
1880 FG = 1:Y1 = 0: FOR TH = 1 TO 8: GOSUB 2235: NEXT TH: RETURN
1999 :
2000 REM DISPLAY TEMP (#)
2001 :
2010 VTAB 24: HTAB (5 * TH - 4)
2020 TP = 25 + TM / 10: REM ***
2021 REM SET BASE TEMP & RANGE
2050 TP$ = CHR$(48 + TP / 10) + CHR$(48 + TP - 10 * INT (TP / 10)) +
".":K = 48 + INT (10 * (TP - INT (TP) + .03))
2052 IF K = 58 THEN K = 48
2054 TP$ = TP$ + CHR$(K)
2060 PRINT TP$;: RETURN
2100 :
2110 REM HANDLE SWITCHING BACK TO PLOT
2120 :
2130 IF X < > 31 THEN RETURN
2140 FG = 0: TEXT : HGR : GOSUB 450:0 = TM: GOTO 800
2200 :
2210 REM DRAW MERCURY
2220 :
2230 Y1 = A%(TH - 1,P - 1)
2235 X = TH * 35 - 18
2240 Y2 = A%(TH - 1,P)
2245 IF Y1 = Y2 THEN RETURN
2250 Z1 = 127 - INT (Y1 / 2 + .1):Z2 = 127 - INT (Y2 / 2 + .1)
2255 IF Z2 = Z1 THEN RETURN
2260 IF Y1 < Y2 THEN HPLOT X,Z1 TO X,Z2: HPLOT X - 1,Z1 TO X - 1,Z2: RETURN
2270 HCOLOR= 0: HPLOT X,Z1 TO X,Z2 - 1: HPLOT X - 1,Z1 TO X - 1,Z2 - 1: HCOL
7: RETURN

```

APPENDIX C — XPRMNT

Variable List:

A%(7,239) = Storage array for temperature data. (8 thermocouples, 240 data points).
B%(7) = Stores temperatures temporarily.
C(7) = Not used.
D\$ = Allows System Commands from BASIC.
J = A temporary variable.
K = A temporary variable.
KB = A keyboard value.
NM = The number of seconds gone by.
PB = Pushbutton number.
PO = Whether to erase old plot before drawing a new one.
PP = Address of switching control.
Q = A temporary variable.
Q(7) = Keeps track of which electrodes have been off.
SN = Slot number the interface board is in.
SP = Whether to store experiment data.
ST = Standard temperature.
TH = Thermocouple number.
TM = Temperature value.
TN = Number of the displayed plot.
TT = Delay loop length.
VA = Indicates whether thermocouple should be on or off.
X = A temporary variable / Keyboard value.
Y = A temporary variable.

APPENDIX C -- "XPRMNT"

(1)

```

80 LOHEM: 24576
90 REM THIS PROGRAM CONTROLS
91 REM     CONTROLS POWER AND
92 REM     RECORDS TEMPERATURE
93 REM     VALUES.
94 REM WHEN TREATMENT IS
95 REM     STOPPED, THE DATA CAN
96 REM     BE GRAPHED,...
100 TEXT : HOME
110 PRINT "HIT S TO STOP TREATMENT."
120 PRINT "IS EVERYTHING READY";: INPUT Q$
132 SN = 4: REM SLOT NUMBER
133 PD = 1: REM WHETHER TO ERASE OLD GRAPH OR PRINT OVER IT
136 PB = 1
138 REM PUSHBUTTON # (THAT IS, FOR THE ONE-BIT INPUT)
142 DIM A$(7,239): DIM Q(7): DIM B$(7): DIM C(7)
143 GOSUB 3000: REM DO TREATMENT
144 HGR : HCOLOR= 7: HOME
145 S = 10
146 TN = 1: REM # OF THE DISPLAYED PLOT
147 GOSUB 450: REM DRAW AXES
149 Q = 1: GOSUB 800
154 :
155 REM MAIN PROGRAM
156 :
157 { 283 X = PEEK (49152): IF X > 127 THEN GOSUB 1000
158 { 286 GOTO 283
159 { 289 :
160 { 290 REM GET TEMPERATURE
161 { 291 :
162 { 292 REM CLEAR PB FLIP FLOP
163 { 293 X = PEEK (49152 + SN * 256)
164 { 298 REM START A=>D ON PROPER
165 { 299 REM THERMOCOUPLE
166 { 300 POKE 49280 + 16 * SN + TH - 1,0
167 { 305 REM 49280=$C080, DVC SELECT
168 { 310 REM WAIT UNTIL READY
169 { 315 X = PEEK (49250)
170 { 320 REM 49248=$C060
171 { 330 IF X < 128 GOTO 315
172 { 340 REM GET THE TEMPERATURE
173 { 350 TH = PEEK (49152 + SN * 256)
174 { 360 REM 49152=$C000, I/O SELECT
175 { 365 RETURN
176 { 449 :
177 { 450 REM DRAW AXES
178 { 451 :
179 { 460 HPLLOT 38,0 TO 38,159: HPLLOT 39,0 TO 39,159: HPLLOT 0,128 TO 279,128: HPL
180 { 0,129 TO 279,129
181 { 470 FOR Y = 1 TO 60: J = 39 + 4 * Y: HPLLOT J,130
182 { 480 IF Y / 10 = INT (Y / 10) THEN HPLLOT J,131 TO J,133
183 { 490 NEXT Y
184 { 500 FOR Y = 127 TO 1 STEP - 5: HPLLOT 37,Y: NEXT Y
185 { 510 FOR Y = 127 TO 1 STEP - 25: HPLLOT 34,Y TO 37,Y: NEXT Y
186 { 515 UTAB 21: HTAB 1: PRINT "USE: 1-8, A/T DOTS, X EXITS, P PRINTS, S SAV
187 { ES SCREEN. NOW #"TN".

```

(2)

```

520 RETURN
800 :
810 REM DRAW A PLOT
815 :
900 FOR X = 0 TO 239:Y = AX(0 - 1,X): IF Y > 255 THEN Y = Y - 256
905 HPLOT 40 + X,127 - INT (Y / 2): NEXT X
910 RETURN
999 :
1000 REM A BUTTON'S BEEN PUSHED
1001 :
1005 POKE 49168,0:X = X - 176
1011 IF X = 40 THEN TEXT : HOME : END
1014 IF X < 9 AND X > 0 THEN 1064
1025 IF X = 17 THEN 1400
1027 IF X = 36 THEN HCOLOR= 0: GOSUB 1400: HCOLOR= 7: RETURN
1028 IF X = 35 THEN PO = - PO
1030 IF X < > 32 THEN RETURN
1035 :
1036 REM SEND GRAPH TO PRINTER
1037 :
1040 UTAB 1: PRINT " ":D$ = CHR$(4)
1050 PRINT D$"PR#1"
1051 FOR X = 1 TO 20: NEXT X
1052 POKE - 12524,0: REM INVERSE
1055 CT = N
1060 PRINT "THERMOCOUPLE #"TN", "S" SECONDS/SAMPLE.": PRINT CHR$(17): PRINT
D$"PR#0": RETURN
1062 :
1064 REM DRAW A NEW PLOT
1066 :
1070 Q = TN:TN = X: IF PO = 1 THEN HCOLOR= 0: GOSUB 800
1075 UTAB 22: HTAB 23: PRINT TN:
1080 Q = TN: HCOLOR= 7: GOTO 800
1400 :
1410 REM ADD POINTS OF CALIBRATION
1420 :
1430 FOR Y = 127 TO 0 STEP - 5: FOR X = 59 TO 279 STEP 20
1440 HPLOT X,Y: NEXT X,Y: RETURN
3000 :
3010 REM DO TREATMENT
3020 :
3040 :
3045 ST = 43.0: REM DEFINE STANDARD TEMPERATURE
3050 PP = 49328
3051 FOR X = 0 TO 7:Q(X) = 0: NEXT X
3052 :
3055 REM KILL POWER
3057 :
3058 NM = NM + 1: REM COUNT # OF SECONDS OF TREATMENT
3059 SP = 0:N1 = NM / 10: IF N1 = INT (N1) THEN SP = 1: REM EVERY TENTH
ONE IS SPECIAL; WE SAVE VALUES.
3060 POKE PP,130
3070 :
3080 REM READ EACH TEMPERATURE
3110 :
3120 FOR TH = 1 TO 8

```

(3)

```

3125 GOSUB 290: REM READ TEMP.
3127 B%(TH - 1) = TM
3130 IF SP = 1 THEN A%(TH - 1,N1 - 1) = TM: REM SAVE EVERY 10 SECOND'S
      WORTH
3132 :
3134 REM COMPARE TO STANDARD
3135 :
3137 UA = 66
3139 C(TH - 1) = 0
3140 IF 30 + TM / 10 > ST THEN UA = 64: C(TH - 1) = 1: C(TH - 1) = 1: IF SP
      = 1 THEN A%(TH - 1,N1 - 1) = TM + 256: REM IF POWER WAS OFF, NOTE
      THAT BY TURNING ON A BIT IN THE MATRIX
3150 :
3160 REM SET UP ELECTRODE'S
3165 REM POWER AS ON OR OFF.
3170 :
3180 POKE PP - 1 + TH,UA
3190 NEXT TH
3200 :
3205 REM CHECK FOR 'STOP,' THEN
3210 REM TURN ON MAIN POWER.
3220 :
3222 KB = PEEK (49152): IF KB > 127 THEN 4000
3225 POKE PP,131
3226 :
3228 REM PRINT VALUES & ON/OFF
3229 :
3230 OU = 0: FOR X = 0 TO 7: IF C(X) = 1 THEN NEXT X: OU = 1
3240 PRINT "SECOND #"NM;: IF OU = 1 THEN PRINT " (SWITCH TO LOW POWER.)"
      ";
3250 PRINT " ": FOR X = 0 TO 7: HTAB (5 * X + 1): PRINT B%(X) / 10 + 30"
      ";: NEXT X
3260 PRINT " ": FOR X = 0 TO 7: Q$ = " OFF ": IF C(X) = 0 THEN Q$ = " ON
      "
3270 PRINT Q$;: NEXT X: PRINT "
3280 PRINT "-----"
3290 :
3300 REM WAIT, & DO IT AGAIN.
3310 :
3315 TT = 50
3320 FOR LP = 1 TO TT: KB = PEEK (49152): IF KB > 127 THEN 4040
3330 NEXT LP: GOTO 3055
4000 :
4010 REM STOP TREATMENT
4020 :
4030 POKE 49168,0: IF KB < > 211 THEN 3225
4040 POKE 49168,0: IF KB < > 211 THEN 3330
4050 RETURN

```

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